

The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: ART108053
Title: An international, multicentre, randomised, double-blind, placebo-controlled, two-parallel group, phase III study to evaluate the efficacy and safety of Arixtra™ (2.5 mg subcutaneously) for the treatment of subjects with acute symptomatic isolated superficial thrombophlebitis of the lower limbs to prevent thromboembolic complications.
Rationale: The common disease pathophysiology in superficial vein thrombosis (SVT) and deep-vein thrombosis (DVT) or pulmonary embolism (PE), and the thromboembolic nature of the main complications of SVT (namely DVT, PE and SVT recurrence or extension), constitute a strong rationale for using anticoagulants in SVT subjects. Previous studies showed that such treatment with unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) may have benefit in this context. Fondaparinux is an anticoagulant agent approved in Europe and the United States for Venous Thromboembolism (VTE) prophylaxis in various clinical settings and the treatment of VTE. The current study ART108053 (CALISTO: Comparison of Arixtra in lower Limbs Superficial vein Thrombosis with placebo), was designed to evaluate the efficacy and safety of fondaparinux versus placebo for the treatment of acute symptomatic isolated SVT (i.e., without concomitant DVT) of the lower limbs to reduce the risk of VTE complications.
Phase: III
Study Period: 23 March, 2007 – 31 July, 2009
Study Design: multicentre, randomised, double-blind, placebo-controlled, two-parallel group
Centres: 171 centres in 17 countries
Indication: Superficial Vein Thrombosis (SVT)
Treatment: Eligible subjects were equally randomised (1:1) into one of two treatment groups: fondaparinux 2.5 mg or matching placebo, administered subcutaneously (SC) once daily (either self administered or not-self administered). The treatment was presented as pre-filled (0.5 mL) syringes. The duration of treatment was 45 days with a 30 day Follow-up period.
Objectives: The primary objective of this study was to evaluate the efficacy of fondaparinux 2.5 mg once daily versus placebo with respect to the occurrence of the primary efficacy endpoint (symptomatic venous thromboembolism [VTE] events and/or death from any cause up to Day 45, end of treatment period) in subjects with isolated SVT (i.e., without concomitant DVT) of the lower limbs. The principal safety objective was to evaluate fondaparinux 2.5 mg once daily versus placebo with respect to the occurrence of major bleeding and/or death up to Day 49 (end of treatment period + 4 days) in subjects with isolated SVT of the lower limbs.
Note: the protocol specified timepoints as up to Day 45 and 75 for efficacy endpoints; however, the analyses included + 2 days (i.e., up to Day 47 and Day 77) to reflect visit windows. For safety endpoints the protocol specified up to Day 49 and Day 75, these were modified to Day 47 or last dose of study drug + 4 days, whichever was longer, and up to Day 77. The revision of the Day 47 time point for safety was to account for subjects with treatment duration longer than 45 days. Adverse events were evaluated 'On-Treatment' defined as from the first study drug injection up to 4 days after the last study drug injection.
Primary Outcome/Efficacy Variable: the incidence of VTE and/or death from any cause recorded up to Day 47. VTE was defined as a composite of symptomatic DVT, symptomatic PE, symptomatic extension of SVT or symptomatic recurrence of SVT. All VTEs were confirmed by objective tests and then adjudicated by an independent central adjudication committee (CAC), whose members were blinded to treatment assignment.
Secondary Outcome/Efficacy Variable(s): Secondary efficacy endpoints included: VTE and/or death from any cause up to Day 77; each component of the primary efficacy endpoint considered separately up to Day 47 and up to Day 77; a composite of symptomatic PE and symptomatic DVT up to Day 47 and up to Day 77; a composite of symptomatic SVT extension and SVT recurrence up to Day 47 and up to Day 77; and surgery to treat SVT up to Day 47 and up to Day 77. Safety endpoints included: the composite of major bleeding and/or death from any cause (primary safety endpoint), major bleeding, clinically relevant non-major bleeding, minor bleeding, and total (any) bleeding (major, clinically relevant non-major and minor bleeding); arterial thromboembolic event (e.g., stroke or myocardial infarction); death from any cause, and any other adverse event (AE). All safety endpoints (except AEs) were evaluated up to Day 47 or day of last injection plus 4 days, whichever was longer, and Day 77. AEs were evaluated during the On-treatment period only. All causes of death (i.e., classified as due to PE, bleeding, cancer, arterial thromboembolic event, infection, or other, reasons), arterial thromboembolic events, and episodes of bleeding (except minor bruising, skin haematomas not

greater than 5 cm in diameter and self-limited episodes of epistaxis or gingival bleeding not necessitating any medical intervention and not associated with any other symptoms) were adjudicated by the CAC.

Statistical Methods: The primary efficacy endpoint was the incidence of adjudicated VTE and/or death from any cause recorded up to Day 47 in the ITT-Population (defined as all randomised subjects). A subject was considered to have a positive evaluation if any one of the following adjudicated outcomes was recorded: all cause death, symptomatic PE, symptomatic DVT, symptomatic recurrence of SVT or symptomatic extension of SVT. For the primary analysis, the two treatment groups were compared using a 2 sided Fisher's exact test at the 5% significance level. The relative risk (RR) and absolute difference (Risk Difference) of the treatment effect was estimated along with the corresponding 95% confidence interval (CI). Subjects with missing VTE status at the timepoint of interest were assumed not to have had a VTE. In addition, an analysis of time to first VTE and/or death was performed to compare the two groups (Kaplan Meier analysis).

The secondary efficacy endpoints defined above were analysed between treatment groups in the same way as the primary efficacy endpoint.

The primary safety endpoint was adjudicated major bleeding and/or death up to Day 47 or day of last injection plus 4 days and up to Day 77 in the As-Treated Population (defined as randomised subjects who received at least one dose of study treatment, as actually received). The number and percentage of subjects reporting a major bleed, clinically relevant non major bleed, minor bleed, and any bleed (major, clinically relevant non major bleed, and minor bleed) were compared between treatment groups using a two-sided Fisher's exact test. The RR and 95% CI for having any bleeding event up until the end of each period were calculated (with the exception of clinically relevant non-major bleeds which were analysed at Day 47 and summarised at Day 77).

Deaths were evaluated both as a component of the combined endpoint of the primary efficacy criterion and as a safety endpoint. It was planned to compare the treatment groups using a two-sided Fisher's exact test, but due to only 3 deaths the analysis was not appropriate.

Study Population: Hospitalised and non-hospitalised male and female subjects 18 years of age or older with acute symptomatic isolated SVT of the lower limbs at least 5 cm long documented by standard compression ultrasound (CUS) were eligible to enter the study. Subjects at high risk of VTE were excluded (e.g., those with DVT on the qualifying ultrasound exam and/or documented PE at inclusion, with SVT within 3 cm from the sapheno-femoral junction [SFJ] requiring ligation of the SFJ or thrombectomy, with active cancer, or with documented DVT or PE within the previous 6 months).

Number of subjects	Fondaparinux	Placebo	Total
Planned	1500	1500	3000
Randomized	1502	1500	3002
Completed, n (%)	1481 (98.6)	1467 (97.8)	2948 (98.2)
Withdrew after randomisation, n (%)	21 (1.4)	33 (2.2)	54 (1.8)
Reason for withdrawal from study			
Withdrawn due to adverse event	2 (0.1)	1 (0.1)	3 (0.1)
Withdrawn due to lack of efficacy	0	0	0
Other	19 (1.3)	32 (2.1)	51 (1.7)
Demographics	Fondaparinux	Placebo	Total
N (ITT)	1502	1500	3002
Females: Males	974: 528	944: 556	1918: 1084
Mean Age, years (SD)	57.1 (13.29)	56.9 (13.56)	57.0 (13.43)
White, European Heritage, n (%)	1485 (98.9)	1492 (99.5)	2977 (99.2)

Primary Efficacy Results (ITT-Population):

Analysis of Incidence of Adjudicated VTE Events and/or Death from any Cause up to Day 47	Fondaparinux N = 1502	Placebo N = 1500
Adjudicated VTE Event and/or Death, n (%)	13 (0.9)	88 (5.9)
Within group CIs ^a	(0.5%, 1.5%)	(4.7%, 7.2%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.148 (0.083, 0.263)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.050 (-0.063, -0.037)	

VTE = Venous Thromboembolism

a. Blyth-Still Casella method.

Secondary Outcome Variables (ITT Population):		
Analysis of Incidence of Adjudicated VTE Events and/or Death from any Cause up to Day 77	Fondaparinux N = 1502	Placebo N = 1500
Adjudicated VTE Event and/or Death, n (%)	18 (1.2)	94 (6.3)
Within group CIs ^a	(0.7%, 1.9%)	(5.1%, 7.6%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.191 (0.116, 0.315)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.051 (-0.064, -0.037)	

VTE = Venous Thromboembolism

a. Blyth-Still Casella method.

Summary of the Incidence of each Adjudicated Component of the Primary Efficacy Endpoint at Each Timepoint	Fondaparinux N = 1502	Placebo N = 1500	Total N = 3002
Day 47			
Number of subjects with adjudicated VTE, n (%)	12 (0.8)	87 (5.8)	99 (3.3)
Death, n (%)	2 (0.1)	1 (0.1)	3 (0.1)
Symptomatic PE, n (%)	0	5 (0.3)	5 (0.2)
Symptomatic DVT, n (%)	3 (0.2)	18 (1.2)	21 (0.7)
Symptomatic recurrence of SVT, n (%)	5 (0.3)	24 (1.6)	29 (1.0)
Symptomatic extension of SVT, n (%)	4 (0.3)	51 (3.4)	55 (1.8)
Day 77			
Number of subjects with adjudicated VTE, n (%)	17 (1.1)	93 (6.2)	110 (3.7)
Death, n (%)	2 (0.1)	1 (0.1)	3 (0.1)
Symptomatic PE, n (%)	0	6 (0.4)	6 (0.2)
Symptomatic DVT, n (%)	4 (0.3)	19 (1.3)	23 (0.8)
Symptomatic recurrence of SVT, n (%)	8 (0.5)	26 (1.7)	34 (1.1)
Symptomatic extension of SVT, n (%)	5 (0.3)	54 (3.6)	59 (2.0)

Note: subjects may have more than 1 event and can be counted in more than 1 category

SVT = Superficial vein thrombosis, PE = Pulmonary embolism, DVT = Deep vein thrombosis

Analysis of Incidence of Adjudicated Symptomatic Pulmonary Embolism at Each Timepoint	Fondaparinux N = 1502	Placebo N = 1500
Day 47		
Symptomatic PE Event, n (%)	0	5 (0.3)
Within group CIs ^a	(0.0%, 0.2%)	(0.1%, 0.8%)
Relative Risk Fondaparinux/Placebo (95% CI)	Not able to calculate ^b	
Fisher's Exact Test, p-value	0.031	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.003 (-0.006, -0.000)	
Day 77		
Symptomatic PE Event, n (%)	0	6 (0.4)
Within group CIs ^a	(0.0%, 0.2%)	(0.2%, 0.8%)
Relative Risk Fondaparinux/Placebo (95% CI)	Not able to calculate ^a	
Fisher's Exact Test, p-value	0.015	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.004 (-0.007, -0.001)	

a. Blyth-Still Casella method.

b. Not able to calculate as the frequency is zero in the fondaparinux group

Analysis of Incidence of Adjudicated DVT at Each Timepoint	Fondaparinux N = 1502	Placebo N = 1500
Day 47		
Symptomatic DVT, n (%)	3 (0.2)	18 (1.2)
Within group CIs ^a	(0.1%, 0.6%)	(0.7%, 1.9%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.166 (0.049, 0.564)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.010 (-0.016, -0.004)	
Day 77		
Symptomatic DVT, n (%)	4 (0.3)	19 (1.3)
Within group CIs ^a	(0.1%, 0.7%)	(0.8%, 2.0%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.210 (0.072, 0.617)	
Fisher's Exact Test, p-value	0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.010 (-0.016, -0.004)	
a. Blyth-Still Casella method.		
Analysis of Incidence of Adjudicated Symptomatic Extension of SVT at Each Timepoint	Fondaparinux N = 1502	Placebo N = 1500
Day 47		
Adjudicated Symptomatic extension of SVT, n (%)	4 (0.3)	51 (3.4)
Within group CIs ^a	(0.1%, 0.7%)	(2.6%, 4.4%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.078 (0.028, 0.216)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.031 (-0.041, -0.022)	
Day 77		
Adjudicated Symptomatic extension of SVT, n (%)	5 (0.3)	54 (3.6)
Within group CIs ^a	(0.1%, 0.8%)	(2.7%, 4.7%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.092 (0.037, 0.231)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.033 (-0.043, -0.023)	
a. Blyth-Still Casella method.		
Analysis of Incidence of Adjudicated Symptomatic Recurrence of SVT at Each Timepoint	Fondaparinux N = 1502	Placebo N = 1500
Day 47		
Adjudicated Symptomatic recurrent SVT, n (%)	5 (0.3)	24 (1.6)
Within group CIs ^a	(0.1%, 0.8%)	(1.0%, 2.4%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.208 (0.080, 0.544)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.013 (-0.020, -0.006)	
Day 77		
Adjudicated Symptomatic recurrent STV, n (%)	8 (0.5)	26 (1.7)
Within group CIs ^a	(0.2%, 1.0%)	(1.1%, 2.5%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.307 (0.140, 0.677)	
Fisher's Exact Test, p-value	0.002	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.012 (-0.020, -0.004)	
a. Blyth-Still Casella method.		

Analysis of Incidence of a Composite of Adjudicated Symptomatic PE and DVT at Each Timepoint	Fondaparinux N = 1502	Placebo N = 1500
Day 47		
Symptomatic PE and DVT, n (%)	3 (0.2)	20 (1.3)
Within group CIs ^a	(0.1%, 0.6%)	(0.8%, 2.0%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.150 (0.045, 0.503)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.011 (-0.018, -0.005)	
Day 77		
Symptomatic PE and DVT, n (%)	4 (0.3)	22 (1.5)
Within group CIs ^a	(0.1%, 0.7%)	(0.9%, 2.2%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.182 (0.063, 0.526)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.012 (-0.019, -0.005)	

a. Blyth-Still Casella method.

Analysis of Incidence of a Composite of Adjudicated Symptomatic SVT Extension or SVT Recurrence at Each Timepoint	Fondaparinux N = 1502	Placebo N = 1500
Day 47		
Symptomatic SVT Extension or SVT Recurrence, n (%)	9 (0.6)	73 (4.9)
Within group CIs ^a	(0.3%, 1.1%)	(3.8%, 6.1%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.123 (0.062, 0.245)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.043 (-0.054, -0.031)	
Day 77		
Symptomatic SVT Extension or SVT Recurrence, n (%)	13 (0.9)	77 (5.1)
Within group CIs ^a	(0.5%, 1.5%)	(4.1%, 6.4%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.169 (0.094, 0.302)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.043 (-0.055, -0.031)	

a. Blyth-Still Casella method.

Analysis of Incidence of the Subjects who required Surgery to Treat SVT Recurrence at Each Timepoint	Fondaparinux N = 1502	Placebo N = 1500
Day 47		
Surgery to treat SVT, n (%)	11 (0.7)	57 (3.8)
Within group CIs ^a	(0.4%, 1.3%)	(2.9%, 4.9%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.193 (0.101, 0.366)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.031 (-0.041, -0.020)	
Day 77		
Symptomatic SVT Extension or SVT Recurrence, n (%)	15 (1.0)	61 (4.1)
Within group CIs ^a	(0.6%, 1.6%)	(3.1%, 5.2%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.246 (0.140, 0.430)	
Fisher's Exact Test, p-value	<0.001	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.031 (-0.042, -0.019)	

a. Blyth-Still Casella method.

Safety Results (As-Treated Population)		
Primary safety endpoint		
Analysis of Incidence of Adjudicated Major Bleeding Event and/or Death at Each Time Point	Fondaparinux N = 1499	Placebo N = 1488
Day 47 or last dose + 4 days		
Any Adjudicated Major Bleeding Event and/or Death, n (%)	3 (0.2)	2 (0.1)
Within group CIs ^a	(0.1%, 0.6%)	(0.0%, 0.5%)
Relative Risk Fondaparinux/Placebo (95% CI)	1.49 (0.25, 8.90)	
Fisher's Exact Test, p-value	1.000	
Risk Difference (Fondaparinux – Placebo) (95% CI)	0.001 (-0.002, 0.004)	
Day 77		
Any Adjudicated Major Bleeding Event and/or Death, n (%)	3 (0.2)	2 (0.1)
Within group CIs ^a	(0.1%, 0.6%)	(0.0%, 0.5%)
Relative Risk Fondaparinux/Placebo (95% CI)	1.49 (0.25, 8.90)	
Fisher's Exact Test, p-value	1.000	
Risk Difference (Fondaparinux – Placebo) (95% CI)	0.001 (-0.002, 0.004)	
Analysis of Incidence of Adjudicated Major Bleeding Event at Each Time Point		
Day 47 or last dose + 4 days		
Any Adjudicated Major Bleeding Event, n (%)	1 (0.1)	1 (0.1)
Within group CIs ^a	(0.0%, 0.4%)	(0.0%, 0.4%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.99 (0.06, 15.86)	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.001 (-0.002, 0.002)	
Day 77		
Any Adjudicated Major Bleeding Event, n (%)	1 (0.1)	1 (0.1)
Within group CIs ^a	(0.0%, 0.4%)	(0.0%, 0.4%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.99 (0.06, 15.86)	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.001 (-0.002, 0.002)	
Analysis of Incidence of Adjudicated Clinically Relevant Non-Major Bleeding Event		
Day 47 or last dose + 4 days		
Any Clinically Relevant Non-Major Bleeding Event, n (%)	5 (0.3)	8 (0.5)
Within group CIs ^a	(0.1%, 0.8%)	(0.2%, 1.0%)
Relative Risk Fondaparinux/Placebo (95% CI)	0.620 (0.203, 1.892)	
Fisher's Exact Test, p-value	0.421	
Risk Difference (Fondaparinux – Placebo) (95% CI)	-0.002 (-0.007, 0.003)	
Day 77		
Any Clinically Relevant Non-Major Bleeding Event, n (%)	6 (0.4)	9 (0.6)
	Not analysed	
Analysis of Incidence of Any (total) Adjudicated Bleeding Event at Each Time Point		
Day 47 or last dose + 4 days		
Any Adjudicated Bleeding Event, n (%)	15 (1.0)	14 (0.9)
Within group CIs ^a	(0.6%, 1.6%)	(0.5%, 1.5%)
Relative Risk Fondaparinux/Placebo (95% CI)	1.06 (0.52, 2.20)	
Fisher's Exact Test, p-value	1.000	
Risk Difference (Fondaparinux – Placebo) (95% CI)	0.001 (-0.006, 0.008)	
Day 77		
Any Adjudicated Bleeding Event, n (%)	16 (1.1)	15 (1.0)
Within group CIs ^a	(0.6%, 1.7%)	(0.6%, 1.6%)
Relative Risk Fondaparinux/Placebo (95% CI)	1.06 (0.53, 2.13)	
Fisher's Exact Test, p-value	1.000	
Risk Difference (Fondaparinux – Placebo) (95% CI)	0.001 (-0.007, 0.008)	
An On-Therapy adverse event (AE) or serious adverse event (SAE) was defined as an AE or SAE with an onset from the first study drug injection up to 4 days after the last study injection.		

Most Frequent Adverse Events – On-Therapy (10 most frequent AEs in each treatment group)	Fondaparinux N = 1499	Placebo N = 1488
Subjects with any AE(s), n(%)	195 (13.0)	199 (13.4)
Headache	34 (2.3)	31 (2.1)
Injection site haematoma	27 (1.8)	17 (1.1)
Hypertension	20 (1.3)	15 (1.0)
Asthenia	14 (0.9)	16 (1.1)
Nasopharyngitis	13 (0.9)	9 (0.6)
Pain in extremity	13 (0.9)	13 (0.9)
Arthralgia	11 (0.7)	11 (0.7)
Abdominal pain	9 (0.6)	5 (0.3)
Diarrhoea	7 (0.5)	12 (0.8)
Backpain	7 (0.5)	7 (0.5)
Vertigo	6 (0.4)	9 (0.6)
Serious Adverse Events - On-Therapy n (%) [n considered by the investigator to be related to study medication]	Fondaparinux N = 1499	Placebo N = 1488
Subjects with any SAEs, n (%)		
Includes both fatal and non-fatal events	10 (0.7)	16 (1.1) [4]
Angina pectoris	0	1 (0.1)
Atrial fibrillation	0	1 (0.1)
Cardiac failure acute	0	1 (0.1)
Coronary artery disease	0	2 (0.1)
Myocardial infarction	0	1 (0.1)
Right ventricular failure	1 (0.1)	0
Gastrointestinal haemorrhage	0	1 (0.1)
Intestinal obstruction	0	1 (0.1)
Billiary colic	0	1 (0.1)
Cholelithiasis	0	1 (0.1)
Erysipelas	0	1 (0.1)
Haematoma infection	0	1 (0.1) [1]
Peritonsillar abscess	0	1 (0.1)
Prostatic abscess	0	1 (0.1)
Staphylococcal infection	0	1 (0.1)
Fall	1 (0.1)	
Road traffic accident	0	1 (0.1)
Fasciitis	0	1 (0.1)
Pain in extremity	1 (0.1)	0
Bile duct cancer	1 (0.1)	0
Pancreatic carcinoma stage IV	1 (0.1)	0
Cerebrovascular accident	0	1 (0.1)
Vertebrobasilar insufficiency	1 (0.1)	0
Renal colic	0	1 (0.1)
Renal cyst	1 (0.1)	0
Urethral obstruction	0	1 (0.1)
Menometrorrhagia	0 (0.1)	1 (0.1) [1]
Chronic obstructive pulmonary disease	1 (0.1)	0
Dermatitis	1 (0.1)	0
Henoch-Schonlein purpura	0	1 (0.1) [1]
Petechiae	0	1 (0.1) [1]
Circulatory collapse	1 (0.1)	0
Hypertensive crisis	0	1 (0.1)
Jugular vein thrombosis	1 (0.1)	0
Subclavian vein thrombosis	1 (0.1)	0
Vena cave thrombosis	1 (0.1)	0

Subjects with fatal SAEs n (%) [n considered by the investigator to be related to study medication]	Fondaparinux N = 1499	Placebo N = 1488
Subjects with fatal SAEs, n (%)	2 (0.1)	1 (0.1)
Cancer	2 (0.1)	0
'Other' (acute heart failure)	0	1 (0.1)
Publications:		
Decousus H for the CALISTO study group: Fondaparinux in the treatment of superficial-vein thrombosis of the lower limbs: A randomized double-blind placebo-controlled study. <i>NEJM</i> (publication pending).		